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Gastrointestinal Bleeding Following LVAD Placement from Top to Bottom

Kelly Cushing, MD and

Washington University, Department of Gastroenterology, 660 South Euclid Ave, St. Louis, MO 63110, kcushing@dom.wustl.edu

Vladimir Kushnir, MD

Washington University, Department of Gastroenterology, 660 South Euclid Ave, St. Louis, MO 63110, vkushnir@dom.wustl.edu

Abstract

Left ventricular assist devices (LVADs) are an increasingly prevalent form of mechanical support for patients with end-stage heart failure. These devices can be implanted both as a bridge to transplant or definitive/destination therapy. Gastrointestinal (GI) bleeding is one of the most common and recalcitrant long-term complications following LVAD implantation, with an incidence approaching 30%.

The pathophysiology of bleeding is multifactorial, with hemodynamic alterations, acquired von Willebrand factor deficiency, and coagulopathy being most often implicated. The majority of bleeding events in this population result from angiodysplasias and gastro-duodenal erosive disease. While these bleeding events are significant and often require transfusion therapy, they are rarely life threatening. Endoscopy remains the standard of care with upper endoscopy offering the highest diagnostic yield in these patients. However, the effectiveness of endoscopic hemostasis in this population is not well established. A small number of studies have evaluated medical therapy and alterations in LVAD settings as a means of preventing or treating bleeding with variable results. In summary, GI bleeding with LVADs is a common occurrence and will continue to be as more LVADs are being performed for destination therapy. This review will discuss what is known about the pathophysiology of GI bleeding in LVADs and the currently available options for medical and/or endoscopic management.

Background

Heart failure affects over 5 million Americans, with numbers expected to rise significantly by 2030. [1] While heart transplantation is the most effective long term strategy, demand for organs supersedes availability. This gap has been increasingly filled by implantation of left ventricular assist devices (LVAD), both as a bridge to transplant and as “destination” therapy.

First generation LVADs were based on a pulsatile flow of blood through the device, mimicking the cardiac cycles of systole and diastole. However, these devices had high rates of post-operative complications and poor durability. The next generation of devices, continuous flow LVADs (CF-LVADs), utilized a central rotor to deliver a non-pulsatile flow

of blood from the left ventricle to the aorta. [2] While both pulsatile and CF-LVADs have led to improved quality of life and functional capacity, CF-LVADs have demonstrated superior survival rates and decreased adverse events. [3] Therefore, CF-LVADs have become the dominant treatment of advanced heart failure.

With the rapid increase in clinical use of LVADs over the last decade, it has become clear that patients experience unusually high rates of gastrointestinal (GI) bleeding following implantation.[4]

Methods

A literature search of Pubmed was performed using the following keywords and/or combination of keywords: [LVAD], [GI bleed], [GI bleeding], [Endoscopy], [Octreotide], [Thalidomide]. The search was restricted to the English language with date range, 1966 to present.

Results

Incidence of Gastrointestinal Bleeding Following LVAD Implantation

The incidence of GI bleeding has been quantified to be 6.8 events/100 patient years or 10% in pulsatile LVADS. [5, 6] CF-LVADS, however, demonstrate an increased incidence of GI bleeding, estimated at 63 events/100 patient years or 20 to 30% [5-7], with recurrent bleeding at 30 to 40%. [4, 8, 9] However, the incidence of bleeding has been reported to be as high as 61% [10] with recurrent bleeding as high as 72% [11].

Risk Factors for Gastrointestinal Bleeding following LVAD Implantation

Many studies have sought to evaluate the clinical and/or demographic characteristics associated with GI bleeding. The only demographic risk factor consistently reported is increased patient age [4, 7, 12-14]. Clinical factors have included preoperative aspirin/ anticoagulation use [12, 14], a history of GI bleeding prior to VAD implantation [8, 15], platelet count [8], an elevated creatinine, right ventricular dysfunction, post LVAD EF>30%, and a lower pulsatility index [7, 9]; however these associations have not been seen uniformly in the literature. Additionally, higher rates of bleeding have been reported when LVADs are placed as destination therapy rather than bridge to transplant; likely a reflection of a higher burden of co-morbidities in the destination therapy population. [14]

Pathophysiology

Early reports ascribed the high rates of GI bleeding to the intensive anticoagulation utilized following LVAD placement. However, the rates of GI bleeding following LVAD placement exceed the rates of GI bleeding seen in patients who are similarly anti-coagulated for other cardiac conditions; implying separate mechanisms or risk factors involved. [4]

A leading hypothesis for LVAD-related GI bleeding centers on alterations in hemodynamics which occur during mechanical support; particularly given the high rates of bleeding seen in patients supported by CF-LVADs vs. pulsatile LVADs. [5-7] The physiologic pulsatility associated with the normal cardiac contraction cycle is lost in CF-LVADs; leading to a

narrowed arterial pulse pressure with decreased aortic valve opening. [16] This clinical scenario closely mimics what is seen in aortic stenosis, which is associated with Heyde's syndrome. [17] Heyde's syndrome is the described association between bleeding gastrointestinal angiodysplasias and aortic stenosis. Patients with aortic stenosis have cessation of GI bleeding following aortic valve replacement. [18] Investigators have also observed that patients who have LVADs have cessation of GI bleeding after cardiac transplantation. [12, 13, 15, 16]

It has been proposed that decreased pulsatility leads to increased bleeding risk via an acquired von Willebrand disease (vWD). Warkentin, et al raised the possibility of a link between acquired vWD and aortic stenosis in 1992. [19] Abnormalities including the loss of high molecular weight multimers, decreased von Willebrand factor (vWF) collagen binding activity, and platelet function abnormalities were subsequently described in aortic stenosis patients. [20] These findings laid the groundwork for further exploring the link between acquired vWD and VADs. Loss of high molecular weight multimers and reduced vWF functional activity were found in patients with VADs when compared to patients who received a heart transplant. [21] These findings were confirmed in a study by Uriel et al, which demonstrated that patients with LVADs had absent or decreased high molecular weight vWF multimers with normalization of multimers after heart transplantation. [22] Finally, reduction in high molecular weight vWF multimers was demonstrated in a patient transitioning from a pulsatile LVAD to a CF-LVAD [23]

The mechanism of loss of high molecular weight vWF multimers is speculated to be from shear forces created by the LVAD causing resultant proteolysis of the multimer. In vitro studies of vWF with tensile forces applied at the A2 site of the multimer have shown selective unfolding with exposure of this domain, facilitating its cleavage. [24] These results offer a possible molecular mechanism for the development of acquired vWD in patients with LVADs. While acquired vWF deficiency has not been proven to be singularly responsible for GI bleeding [25], it may contribute to an increased propensity to bleed.

Finally, impaired platelet aggregation has been suggested as a contributing mechanism in the association of LVADs with GI bleeding. In one recent report, seven of eleven LVAD patients tested had impaired ability of both plasma and platelet factors to mediate ristocetin induced platelet aggregation. Platelet aggregation was also found to have normalized after heart transplantation. [26]

Continuous flow devices cause lowered pulse pressure with relative hypoperfusion of the gut, a systemic decrease in high molecular weight vWF multimers, and impaired platelet aggregation. These factors likely lead to development of angiodysplasias and an increased risk of bleeding from these angiodysplasias. [27]

Clinical Presentation

The reported time to the first bleeding event ranges from 87 to 159 days following LVAD implantation. [12, 14] The majority of patients present from an outpatient setting; fewer than 15% of patients are hemodynamically unstable at time of presentation. [14] The majority of bleeding events resolve within 4 days and patients require an average of three to four units of

packed red blood cells (PRBCs) per bleeding event. [10, 12, 14, 15] Overt, upper GI bleeding is the most frequent presentation with 50% of patients reporting passage of melanic stools. [4, 10, 14]

Multiple studies have evaluated the location and etiology of bleeding in this patient population. The upper GI tract is more often identified as the source of bleeding (40-50%), followed by the colon in 22% of patients, small bowel in 15% and obscure source of bleeding in 19%. [7][11] The available evidence suggests that the middle GI tract is where a majority of obscure bleeding events originate. The most frequent endoscopic findings are angiodysplasias and peptic disease. [4, 7, 9-11, 13, 14]

Endoscopic Evaluation and Management

Endoscopy is the mainstay of the initial evaluation and treatment of LVAD related GI bleeding. The diagnostic yield of conventional endoscopic workup in these patients is approximately 60 to 80% [14, 28, 29] with upper endoscopy offering the highest yield. [10, 14] (Table 1)

The data on device-assisted enteroscopy (DAE) which includes single balloon, double balloon, and spiral enteroscopy is more limited. Edwards, et al recently reported an initial experience with the use of early antegrade double balloon enteroscopy in patients with LVADs who had a negative conventional endoscopic workup or positive capsule findings. Thirteen procedures were performed, which were predominantly antegrade in approach. The bleeding source was identified in 9 of 13 procedures achieving a diagnostic yield of 69%. [30] Timing of device-assisted enteroscopy (DAE), specifically deep-overtube assisted enteroscopy, has also been retrospectively evaluated. Patients with LVAD related GI bleeding were subgrouped into 1) traditional endoscopic workup 2) late DAE, after traditional workup or 3) early DAE, within 24 hours. Comparative analysis revealed that early DAE was associated with decreased transfusion requirements, decreased number of days to treatment, and decreased number of diagnostic tests performed. [11] These results support early small bowel evaluation to maximize diagnostic and therapeutic yield.

The ACG and the ASGE have published recommendations supporting capsule endoscopy prior to DAE for initial evaluation of suspected small bowel bleeding/obscure GI bleeding. Capsule endoscopy before DAE allows for targeted therapy providing endoscopists with an estimated location of bleeding, optimal route, and improved diagnostic yield. [31, 32] The diagnostic yield of capsule endoscopy has been noted to be as low as 20% [14] and as high as 100% in the LVAD population.[33] When capsule endoscopy is abnormal, the most frequent finding is blood in the lumen of the gastrointestinal tract. However, the culprit lesion is directly visualized less than 25% of the time.[33] This suggests capsule endoscopy can help localize the site of bleeding with VCE but may not visualize the principal bleeding angiodysplasia.

When lesions with high risk bleeding stigmata are identified, endoscopic maneuvers are successful in initial hemostasis in 80 to 90% of patients; however re-bleeding despite endoscopic therapy is not uncommon and occurs in up to 50% [28, 29] There have been no clear studies performed to evaluate for superiority of one endoscopic treatment option over

another. Most reports describe use of argon plasma coagulation (APC), contact coagulation, epinephrine and hemoclips in this population, with choice of modality driven by the etiology of bleeding.

Capsule endoscopy can be safely pursued in patients with LVADs, ICDs and/or pacemakers. [34, 35] It is important to note, however, that there has been some evidence of brief interference with capsule image acquisition when the capsule device is in the upper abdomen, which is postulated to be secondary to being in close proximity to the LVAD. [35] Several studies have evaluated the safety of flexible endoscopy during LVAD support. [30, 34] Both moderate and deep sedation have been shown to be relatively safe with limited iatrogenic complications. [14, 36][37][38]

Medical Management

The universal strategies for managing GI bleeds apply in all populations, including those with LVADs. These interventions include large bore IV access, PRBC transfusion for significant anemia, acid suppression for melena, and hemodynamic support if instability is present. Hemodynamic monitoring and fluid management can be challenging in the LVAD population, requiring close collaboration across disciplines.

Given that the LVAD population has a unique pathophysiology contributing to recurrent GI bleeding as well as the concurrent need for long term anticoagulation, medical strategies specific to the LVAD population are needed. One strategy which has been investigated is to increase the pulsatility of the device, thus the aortic valve opening, by reducing the speed. The role of low pulsatility in the risk of nonsurgical bleeding was demonstrated by Wever-Pinzon and colleagues. [39] However, this strategy has not been widely adopted among VAD centers given its predominantly anecdotal evidence. With lowering the flow of the device, there is an increased concern for thromboembolic events, particularly when patients also require cessation of anticoagulation.

The management of anticoagulation in LVAD patients continues to evolve with increased understanding of the long term risk of bleeding as well as device related thromboembolic events. A multi-center evaluation of reduced anticoagulation strategies (TRACE) demonstrated risk of device thrombosis and ischemic stroke in those on reduced anticoagulation regimens following a bleeding event. Notably, there were still 71 major bleeding events despite the reduced anticoagulation. [40] It has been shown that thromboembolic events are 7 times as likely in patients with GI bleeding events. [41] However, a retrospective review by Kamdar et al evaluated 14 patients with GI bleeding and cessation of anticoagulation and found that one patient had a pump thrombosis necessitating device exchange over a mean duration of 392 days off warfarin. [42] Moreover, the intensity of anticoagulation has not consistently been linked to risk of gastrointestinal bleeding in the LVAD population. The complexity of medical decision making in this area, in which there is a lack of clear cut evidence, highlights the importance of a multidisciplinary approach to managing GI bleeds in this patient population.

Strategies utilized for LVAD related bleeding have been derived from the medical management of angiodysplasias. (Table 2) Octreotide, a somatostatin analogue involved in

decreased acid secretion/splanchnic flow, inhibition of angiogenesis and platelet aggregation, has been shown to stabilize GI bleeding in patients with LVADs in multiple case reports. [43][44-46] However, in larger case series, octreotide did not appear to significantly impact the rate of recurrent GI bleeding or decrease the need for transfusion. [8, 47]. In the acute setting, Hayes et al used a combination of reduction in pump flow, adrenaline infusions and octreotide with success in 5 patients with GI bleeding. [48] Adverse events during octreotide administration have been limited to diarrhea and abdominal cramps.

Thalidomide has also been evaluated in several small studies; given its known anti-angiogenic properties and reports of efficacy in treating angiodysplasia related GI bleeding in other populations. [49-52] In 2014, Ray et al documented a case report of a patient with a CF-LVAD who developed recurrent bleeding from upper and lower GI tract angiodysplasias despite APC therapy. The patient was started on thalidomide 50mg twice daily given his need for anticoagulation in the setting of recurrent bleeding. No bleeding was noted at 1 year. [53] The same group subsequently published an algorithm for prescribing thalidomide in patients with LVADs and recurrent bleeding. Implementation of this algorithm at their institution was associated with reduced bleeding events. There were, however, notable adverse effects including symptomatic neuropathy. Two patients also died of sepsis in this small cohort. [54]

Thalidomide has strict regulations regarding its prescription and dispensal. Currently, physicians using thalidomide must belong to the THALOMID Risk Evaluation and Mitigation Strategy (REMS) Program in order to prescribe the medication. There is also an established risk of thrombosis with the use of thalidomide raising a question of its safety in patients with implanted mechanical devices. Overall, there is very little data regarding the use of thalidomide in this population and thus there are no clear guidelines on use of this medication in the LVAD population.

A recent study documented the use of Wilfactin, vWF concentrate devoid of factor VIII, in a CF-LVAD patient with severe GI bleeding. This led to stabilization of hemoglobin and cessation of bleeding without thromboembolic complications. The patient was notably also started on octreotide for anemia secondary to angiodysplasias which were diagnosed later in the hospital course. [55] While most patients with LVADs have non-life threatening bleeding which does not require coagulopathy reversal agents, this case report offers a possible area for further research in situations where more severe bleeding is encountered necessitating coagulopathy reversal and when thromboembolic risk needs to be reduced.

Finally, there has been one published case report on the use of danazol in an LVAD patient with refractory GI bleeding. Danazol is an androgen that has been demonstrated to have possible benefit in the management of refractory bleeding from intestinal angiodysplasias. [56] This patient had clear evidence of angiodysplasias endoscopically with recurrence despite hemostatic measures. Danazol was started at a dose of 200mg twice daily. Therapy was ultimately limited by rising creatinine. However, it is notable that for 9 months, the patient had no major bleeding episodes. [57] Important side effects include drug induced liver toxicity and thromboembolic events.

Impact on Patient Outcomes

Bleeding events can be a significant cause of morbidity, as evidenced by being a leading cause of readmission [58] with patients averaging three to four units of PRBCs per bleeding event. [10, 12, 14, 15] The high consumption of blood products for recurrent bleeders can be associated with a risk of allosensitization, which is important in patients who are transplant candidates. Patients may also require cessation of anticoagulation increasing the risk of thromboembolic events. [41] While morbidity is significant, mortality is not. Survival analysis, compared between patients with and without GI bleeding, did not show a statistically significant difference. [15]

Approach to Management

Based on our review of the literature, we propose a diagnostic algorithm for LVAD related GI bleeding. (Figure 1) The first assessment should be for stability, with resuscitation efforts in the unstable patient. For those who are too unstable for endoscopy, angiography and embolization are alternative diagnostic and therapeutic choices. Based on available data, we feel that push enteroscopy should be the initial endoscopic procedure utilized; given the high likelihood of upper GI tract angiodysplasias. If push enteroscopy is unrevealing, the conventional endoscopic workup should be completed. VCE should then be considered in order to localize the source of bleeding, risk stratify the patient and guide further endoscopic interventions. Additional diagnostic evaluations such as deep enteroscopy and tagged RBC scans should be utilized based on clinical picture and pre-test probability. In those patients with recurrent GI bleeding from demonstrated angiodysplasias, a trial of octreotide can be considered, given its favorable side effect profile. Finally, in a highly selected cohort of patients with chronic, occult GI bleeding, outpatient management could be considered. Outpatient treatment failure occurred 13.3% of the time in a study by Raymer, et al. [59] However, this has only been studied retrospectively and has only been presented in abstract form. Therefore, further prospective studies should be performed.

Significance

As the field of cardiology advances forward with artificial assist devices for end stage heart failure, the short and long term impact on other organ systems will become more evident. LVADs have clear gastrointestinal effects likely related to the mechanics of the device itself as well as its resultant physiology, which impact the gut vasculature as well as the hematologic system. It is important to understand the mechanism and clinical pattern of GI bleeding in these patients as it is prevalent, often requires endoscopic management, and requires coordinated care with expert cardiologists.

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Bibliographie

1. Mozaffarian D, et al. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. *Circulation*. 2015; 131(4):e29–322. [PubMed: 25520374]

2. Loor G, Gonzalez-Stawinski G. Pulsatile vs. continuous flow in ventricular assist device therapy. *Best Pract Res Clin Anaesthesiol.* 2012; 26(2):105–15. [PubMed: 22910084]
3. Slaughter MS, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med.* 2009; 361(23):2241–51. [PubMed: 19920051]
4. Shrode CW, et al. Significantly higher rates of gastrointestinal bleeding and thromboembolic events with left ventricular assist devices. *Clin Gastroenterol Hepatol.* 2014; 12(9):1461–7. [PubMed: 24480675]
5. Crow S, et al. Gastrointestinal bleeding rates in recipients of nonpulsatile and pulsatile left ventricular assist devices. *J Thorac Cardiovasc Surg.* 2009; 137(1):208–15. [PubMed: 19154927]
6. Islam S, et al. Left ventricular assist devices and gastrointestinal bleeding: a narrative review of case reports and case series. *Clin Cardiol.* 2013; 36(4):190–200. [PubMed: 23378047]
7. Draper KV, Huang RJ, Gerson LB. GI bleeding in patients with continuous-flow left ventricular assist devices: a systematic review and meta-analysis. *Gastrointest Endosc.* 2014; 80(3):435–446. [PubMed: 24975405]
8. Aggarwal A, et al. Incidence and management of gastrointestinal bleeding with continuous flow assist devices. *Ann Thorac Surg.* 2012; 93(5):1534–40. [PubMed: 22541185]
9. Jabbar HR, et al. The Incidence, Predictors and Outcomes of Gastrointestinal Bleeding in Patients with Left Ventricular Assist Device (LVAD). *Dig Dis Sci.* 2015
10. Marsano J, et al. Characteristics of gastrointestinal bleeding after placement of continuous-flow left ventricular assist device: a case series. *Dig Dis Sci.* 2015; 60(6):1859–67. [PubMed: 25616611]
11. Sarosiek K, et al. An old problem with a new therapy: gastrointestinal bleeding in ventricular assist device patients and deep overtube-assisted enteroscopy. *Asaio j.* 2013; 59(4):384–9. [PubMed: 23820277]
12. Stern DR, et al. Increased incidence of gastrointestinal bleeding following implantation of the HeartMate II LVAD. *J Card Surg.* 2010; 25(3):352–6. [PubMed: 20331479]
13. Demirozu ZT, et al. Arteriovenous malformation and gastrointestinal bleeding in patients with the HeartMate II left ventricular assist device. *J Heart Lung Transplant.* 2011; 30(8):849–53. [PubMed: 21530318]
14. Kushnir VM, et al. Evaluation of GI bleeding after implantation of left ventricular assist device. *Gastrointest Endosc.* 2012; 75(5):973–9. [PubMed: 22341716]
15. Morgan JA, et al. Gastrointestinal bleeding with the HeartMate II left ventricular assist device. *J Heart Lung Transplant.* 2012; 31(7):715–8. [PubMed: 22425231]
16. Letsou GV, et al. Gastrointestinal bleeding from arteriovenous malformations in patients supported by the Jarvik 2000 axial-flow left ventricular assist device. *J Heart Lung Transplant.* 2005; 24(1):105–9. [PubMed: 15653390]
17. Heyde EC. GASTROINTESTINAL BLEEDING IN AORTIC STENOSIS. *New England Journal of Medicine.* 1958; 259(4):196–196.
18. Cappel MS, Lebowitz O. Cessation of recurrent bleeding from gastrointestinal angiodysplasias after aortic valve replacement. *Ann Intern Med.* 1986; 105(1):54–7. [PubMed: 3487267]
19. Warkentin TE, Moore JC, Morgan DG. Aortic stenosis and bleeding gastrointestinal angiodysplasia: is acquired von Willebrand's disease the link? *Lancet.* 1992; 340(8810):35–7. [PubMed: 1351610]
20. Vincentelli A, et al. Acquired von Willebrand syndrome in aortic stenosis. *N Engl J Med.* 2003; 349(4):343–9. [PubMed: 12878741]
21. Geisen U, et al. Non-surgical bleeding in patients with ventricular assist devices could be explained by acquired von Willebrand disease. *Eur J Cardiothorac Surg.* 2008; 33(4):679–84. [PubMed: 18282712]
22. Uriel N, et al. Acquired von Willebrand syndrome after continuous-flow mechanical device support contributes to a high prevalence of bleeding during long-term support and at the time of transplantation. *J Am Coll Cardiol.* 2010; 56(15):1207–13. [PubMed: 20598466]
23. Malehsa D, et al. Acquired von Willebrand syndrome after exchange of the HeartMate XVE to the HeartMate II ventricular assist device. *Eur J Cardiothorac Surg.* 2009; 35(6):1091–3. [PubMed: 19303790]

24. Baldauf C, et al. Shear-induced unfolding activates von Willebrand factor A2 domain for proteolysis. *J Thromb Haemost*. 2009; 7(12):2096–105. [PubMed: 19817991]
25. Meyer AL, et al. Acquired von Willebrand syndrome in patients with a centrifugal or axial continuous flow left ventricular assist device. *JACC Heart Fail*. 2014; 2(2):141–5. [PubMed: 24720921]
26. Klovait J, et al. Severely impaired von Willebrand factor-dependent platelet aggregation in patients with a continuous-flow left ventricular assist device (HeartMate II). *J Am Coll Cardiol*. 2009; 53(23):2162–7. [PubMed: 19497443]
27. Suarez J, et al. Mechanisms of bleeding and approach to patients with axial-flow left ventricular assist devices. *Circ Heart Fail*. 2011; 4(6):779–84. [PubMed: 22086831]
28. Elmunzer BJ, et al. Endoscopic findings and clinical outcomes in ventricular assist device recipients with gastrointestinal bleeding. *Dig Dis Sci*. 2011; 56(11):3241–6. [PubMed: 21792619]
29. Meyer MM, et al. Endoscopic evaluation and management of gastrointestinal bleeding in patients with ventricular assist devices. *Gastroenterol Res Pract*. 2012; 2012:630483. [PubMed: 22474445]
30. Edwards AL, et al. Utility of double-balloon enteroscopy in patients with left ventricular assist devices and obscure overt gastrointestinal bleeding. *Endoscopy*. 2014; 46(11):986–91. [PubMed: 25290096]
31. Gerson LB, et al. ACG Clinical Guideline: Diagnosis and Management of Small Bowel Bleeding. *Am J Gastroenterol*. 2015; 110(9):1265–1287. [PubMed: 26303132]
32. Khashab MA, et al. The role of deep enteroscopy in the management of small-bowel disorders. *Gastrointest Endosc*. 2015; 82(4):600–7. [PubMed: 26253015]
33. Truss WD, et al. Early Implementation of Video Capsule Enteroscopy in Patients with Left Ventricular Assist Devices and Obscure Gastrointestinal Bleeding. *Asaio j*. 2015
34. Daas AY, et al. Safety of conventional and wireless capsule endoscopy in patients supported with nonpulsatile axial flow Heart-Mate II left ventricular assist device. *Gastrointest Endosc*. 2008; 68(2):379–82. [PubMed: 18582876]
35. Harris LA, et al. Capsule Endoscopy in Patients with Implantable Electromedical Devices is Safe. *Gastroenterol Res Pract*. 2013; 2013:959234. [PubMed: 23710168]
36. Barbara DW, et al. Peri-procedural Management of 172 Gastrointestinal Endoscopies in Left Ventricular Assist Device Patients. *Asaio j*. 2015
37. Kushnir VM, et al. Incidence of Sedation Related Adverse Events (Srae) During Endoscopy in Patients Supported by Continuous Flow Left Ventricular Assist Devices (LVAD). *Gastrointest Endosc*. 2013; 77(5s):AB477.
38. Goudra BG, Singh PM. Anesthesia for gastrointestinal endoscopy in patients with left ventricular assist devices: initial experience with 68 procedures. *Ann Card Anaesth*. 2013; 16(4):250–6. [PubMed: 24107691]
39. Wever-Pinzon O, et al. Pulsatility and the risk of nonsurgical bleeding in patients supported with the continuous-flow left ventricular assist device HeartMate II. *Circ Heart Fail*. 2013; 6(3):517–26. [PubMed: 23479562]
40. Katz JN, et al. Safety of reduced anti-thrombotic strategies in HeartMate II patients: A one-year analysis of the US-TRACE Study. *J Heart Lung Transplant*. 2015; 34(12):1542–8. [PubMed: 26277569]
41. Stulak JM, et al. Gastrointestinal bleeding and subsequent risk of thromboembolic events during support with a left ventricular assist device. *J Heart Lung Transplant*. 2014; 33(1):60–4. [PubMed: 24021944]
42. Kamdar F, Eckman P, John R. Safety of discontinuation of anti-coagulation in patients with continuous-flow left ventricular assist devices. *J Heart Lung Transplant*. 2014; 33(3):316–8. [PubMed: 24462558]
43. Szilagyi A, Ghali MP. Pharmacological therapy of vascular malformations of the gastrointestinal tract. *Can J Gastroenterol*. 2006; 20(3):171–8. [PubMed: 16550261]
44. Rennyson SL, et al. Octreotide for left ventricular assist device-related gastrointestinal hemorrhage: can we stop the bleeding? *Asaio j*. 2013; 59(4):450–1. [PubMed: 23820288]
45. Coutance G, et al. Octreotide for recurrent intestinal bleeding due to ventricular assist device. *Asian Cardiovasc Thorac Ann*. 2014; 22(3):350–2. [PubMed: 24585917]

46. Dang G, et al. Octreotide for the Management of Gastrointestinal Bleeding in a Patient with a HeartWare Left Ventricular Assist Device. *Case Rep Cardiol.* 2014; 2014:826453. [PubMed: 25587457]
47. Loyaga-Rendon RY, et al. Octreotide in the management of recurrent gastrointestinal bleed in patients supported by continuous flow left ventricular assist devices. *Asaio j.* 2015; 61(1):107–9. [PubMed: 25232774]
48. Hayes HM, et al. Management options to treat gastrointestinal bleeding in patients supported on rotary left ventricular assist devices: a single-center experience. *Artif Organs.* 2010; 34(9):703–6. [PubMed: 20883388]
49. Shurafa M, Kamboj G. Thalidomide for The Treatment of Bleeding Angiodysplasias. *Am J Gastroenterol.* 2003; 98(1):221–222. [PubMed: 12526972]
50. Alam MA, Sami S, Babu S. Successful treatment of bleeding gastro-intestinal angiodysplasia in hereditary haemorrhagic telangiectasia with thalidomide. *BMJ Case Rep.* 2011; 2011
51. Ge ZZ, et al. Efficacy of thalidomide for refractory gastrointestinal bleeding from vascular malformation. *Gastroenterology.* 2011; 141(5):1629–37. e1–4. [PubMed: 21784047]
52. Chen CH, et al. Long-term therapy with thalidomide in hereditary hemorrhagic telangiectasia: case report and literature review. *J Clin Pharmacol.* 2012; 52(9):1436–40. [PubMed: 22031620]
53. Ray R, et al. Treatment of left ventricular assist device-associated arteriovenous malformations with thalidomide. *Asaio j.* 2014; 60(4):482–3. [PubMed: 24830804]
54. Draper K, et al. Thalidomide for treatment of gastrointestinal angiodysplasia in patients with left ventricular assist devices: case series and treatment protocol. *J Heart Lung Transplant.* 2015; 34(1):132–4. [PubMed: 25447569]
55. Fischer Q, et al. Von Willebrand factor, a versatile player in gastrointestinal bleeding in left ventricular assist device recipients? *Transfusion.* 2015; 55(1):51–4. [PubMed: 25052086]
56. Botero JP, Pruthi RK. Refractory bleeding from intestinal angiodysplasias successfully treated with danazol in three patients with von Willebrand disease. *Blood Coagul Fibrinolysis.* 2013; 24(8): 884–6. [PubMed: 23867344]
57. Schettle SD, Pruthi RK, Pereira NL. Continuous-flow left ventricular assist devices and gastrointestinal bleeding: potential role of danazol. *J Heart Lung Transplant.* 2014; 33(5):549–50. [PubMed: 24630863]
58. Hasin T, et al. Readmissions after implantation of axial flow left ventricular assist device. *J Am Coll Cardiol.* 2013; 61(2):153–63. [PubMed: 23219299]
59. Raymer D, et al. Outpatient Management of Gastrointestinal Bleeding in Patients with Continuous-Flow Left Ventricular Assist Devices. *J Card Fail.* 2014; 20(8S):084.

KEY POINTS

- LVADs are associated with GI bleeding in approximately 20 to 30% of cases with recurrent bleeding in 30 to 40%
- Melena is the most often observed manifestation of bleeding, with angiodysplasia and gastro-duodenal erosive disease being the predominant etiologies
- Bleeding is likely multifactorial and related to lowered pulse pressure with relative hypoperfusion of the gut, a systemic decrease in high molecular weight von Willebrand factor multimers, and impaired platelet aggregation
- Conventional and wireless capsule endoscopy is safe in patients with LVADs. Upper endoscopy offers the highest diagnostic yield. Early VCE can help localize the source of bleeding, risk stratify the patient and guide further endoscopic interventions.
- Octreotide is an option for advanced medical management but has not yet been proven to be clinically impactful in a large cohort of patients. Thalidomide has not yet been studied extensively enough to make conclusions.
- LVADs and GI bleeding are clinically significant events and will become a common clinical scenario in academic and community practice as more LVADs are being implanted

Figure 1.
Algorithm for Management of GI Bleeding in the LVAD Population

Table 1

Diagnostic Yield of Endoscopic and Radiologic Procedures

Procedure	Diagnostic Yield	References(s)
EGD	37.5-57%	Elmunzer 2011, Meyer 2012, Kushnir 2012, Marsano 2015
Push Enteroscopy	11-30%	Kushnir 2012, Marsano 2015
Colonoscopy	0-46.7%	Elmunzer 2011, Meyer 2012, Kushnir 2012
Deep Enteroscopy	69-100%	Elmunzer 2011, Edwards 2014
Video Capsule Endoscopy	20-100%	Elmunzer 2011, Meyer 2012, Kushnir 2012, Truss 2015
Tagged RBC Scan	50-6C	Elmunzer 2011, Kushnir 2012
Angiography	0%	Elmunzer 2011, Kushnir 2012

Table 2

Published Literature on the Medical Management of GI Bleeding in LVAD patients

Authors	Patients Treated	Medication/Dose	Recurrent GI Bleeding	Adverse Events
Rennyson, et al	1	Octreotide 100µg SQ BID transitioned to 20 mg IM q30 days	Two episodes in 6 months (One attributed to noncompliance with medication)	TIA (discontinued coumadin for 14 days)
Dang, et al	1	Octreotide 100µg SQ BID transitioned to 20mg IM q30 days	One episode in 11 weeks	Not Reported
Coutance, et al	1	Octreotide 100 µg TID transitioned to 30mg SQ qmonth	No GI bleeding events at 23 months	Not reported
Loyaga-Rendon, et al	7	Octreotide 50µg SQ BID or 20mg SC qmonth	Non-significant reduction in hospitalizations related to GIB, PRBCs transfused and number of endoscopies at 3 months **After exclusion of one outlier	Abdominal Cramps Diarrhea
Aggarwal, et al	10	Octreotide continuous infusion or SQ injection	No difference in length of stay, rebleeding episodes, units of PRBCs or mortality	None Reported
Hayes, et al	5	Octreotide 25µg/min IV, 100µg SQ BID or 10mg IM qmonth (with reduction in pump speed, adrenaline infusions)	Bleeding Events were successfully treated	None Reported
Draper, et al	8	Thalidomide 50mg BID (Titrated by algorithm)	5 of 8 patients had no recurrence of bleeding; 2 of 8 patients had reduction of bleeding; One patient died within one week of initiation	Symptomatic Neuropathy, Sepsis
Ray, et al	1	Thalidomide 50mg BID	No recurrent bleeding at 1 year	Not reported
Fischer, et al	1	Wilfactin (vWF concentrate) 7000 IU (80 IU/kg)	Resolution of bleeding event; 1 recurrent bleeding event and the patient was started on octreotide SQ daily	Not reported
Schettle, et al	1	Danazol 200mg BID	No recurrent bleeding for 9 months	None Reported